```
=> d his
```

```
(FILE 'HOME' ENTERED AT 11:21:26 ON 27 JUN 2002)
      FILE 'HCAPLUS' ENTERED AT 11:21:33 ON 27 JUN 2002
                  E ANDO HO?/AU
L1
               14 S E8-9
                  E BUTLER DO?/AU
               77 S E6-8
L2
                  E DOZEMAN G?/AU
                                                                     Twentor
                6 S E4-5
L3
                1 S L1 AND L2 AND L3
L4
L5
               95 S L1 OR L2 OR L3
                1 S L5 AND VASCULAR
L6
L7
                1 S L4 OR L6
                1 S L5 AND DIABETES
L8
                   SELECT L8 1 RN
      FILE 'REGISTRY' ENTERED AT 11:26:02 ON 27 JUN 2002
L9
                8 S E1-8
      FILE 'HCAPLUS' ENTERED AT 11:26:12 ON 27 JUN 2002
                1 S L8 AND L9
L10
      FILE 'REGISTRY' ENTERED AT 12:01:08 ON 27 JUN 2002
L11
                  STR
      FILE 'HCAPLUS' ENTERED AT 12:04:46 ON 27 JUN 2002
      FILE 'REGISTRY' ENTERED AT 12:07:20 ON 27 JUN 2002
                  SAVE L13 REY617A/A
                  SAVE L11 REY617STR/L
L12
                  STR L11
L13
                0 S L12
L14
                  SCREEN 2008
L15
                  SCREEN 1838 OR 1992 OR 2016 OR 2026 OR 2021 OR 2043
L16
                0 S L12 AND L14 NOT L15
L17
                  STR L11
L18
                0 S L17
L19
                0 S L17 AND L14 NOT L15
                  E HEXANOIC ACID, 6/CN
                  E HEXANOIC ACID, 6,6-OXYBIS/CN
               13 S "6,6'-OXYBIS[2,2-DIMETHYL-"
L20
                                                                       Searched via
Inomenclature
                9 S "HEXANOIC ACID, 6,6'-OXYBIS[2,2-DIMETHYL-"
L21
                  E HEPTANOIC ACID
                  E HEPTANOIC ACID/CN
                  E PENTANOIC/CN
L22
                1 S E4
                2 S "PENTANOIC ACID, 5,5'-OXYBIS[2,2-DIMETHYL-"
L23
                1 S "HEPTANOIC ACID, 7,7'-OXYBIS[2,2-DIMETHYL-"
L24
               12 S L21 OR L23 OR L24
L25
                  SAVE L25 REY617NOM/A
      FILE 'HCAPLUS' ENTERED AT 14:54:43 ON 27 JUN 2002 PAR Rlue via nomenclature search

14 S L26 - attached -14 cits from the land printered

4 S L27 AND (CA OR CALC?) - highlighted on attached printered

0 S L27 AND (H20 OR ?HYDRAT?)
L26
L27
L28
L29
```

L30 L31	FILE	'REGISTRY' ENTERED AT 14:57:59 ON 27 JUN 2002 7 S L26 AND "CALCIUM SALT" 1 S L26 AND "H20"  Aughlighted
L33	FILE	1 S L26 AND "H20"  'HCAPLUS' ENTERED AT 15:00:30 ON 27 JUN 2002  5 S L27 AND PREP?  'CAOLD' ENTERED AT 15:05:35 ON 27 JUN 2002
L34	FILE	'CAOLD' ENTERED AT 15:05:35 QN 27 JUN 2002  0 S L26 — Zerohits in CAOLd
L35	FILE	'BEILSTEIN' ENTERED AT 15:05:54 ON 27 JUN 2002 0 S L27—Zerohitz in Beilstein
L36	FILE	'REGISTRY' ENTERED AT 15:08:25 ON 27 JUN 2002  O S L26 AND "?HYDRATE?"  SAVE L26 REY617REG/A  SAVE L30 REY617HCA/A  SAVE L30 REY617REGCA/A  SAVE L31 REY617REGH2O/A

FILE 'HCAPLUS' ENTERED AT 15:12:15 ON 27 JUN 2002 SAVE L27 REY617HCACITS/A REY617HCA/A

Also searched via structure - see done and search history on following pages.

Nomenclature and structure searches

Contained The same results (13 hits),

contained The same results (13 hits),

except that nomenclature search

setrieved an addnl. hit - so all

retrieved an addnl. hit - so all

REP G1=(3-5) CH2 NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE 'L2 ( 11)SEA FILE=REGISTRY SSS FUL L1

```
=> d his
```

L6

L7

Γ8

L9

. . . . . .

```
(FILE 'HOME' ENTERED AT 12:21:21 ON 28 JUN 2002)
                         DELETE HAR034CLU/A
                         DEL HARO34HCA/A
                         DEL HARO34INV/A
                         DEL HARO34MEDL/A
                         DEL HAR897INVHCA/A
                         DEL HAR944CLU/A
       FILE 'HCAPLUS' ENTERED AT 12:24:36 ON 28 JUN 2002
                        ACT REY617MARY/A
                   STR

11) SEA FILE=REGISTRY SSS FUL L1 - // compda in Reg.

13 SEA FILE=HCAPLUS L2 -/3 ait's in HCAPLUS - all mere in

ACT REY617HCA/A nomenolature search results
L1
L2 (
L3
                    9) SEA FILE=REGISTRY "HEXANOIC ACID, 6,6'-OXYBIS[2,2-DIMETHYL-" 2) SEA FILE=REGISTRY "PENTANOIC ACID, 5,5'-OXYBIS[2,2-DIMETHYL-" 1) SEA FILE=REGISTRY "HEPTANOIC ACID, 7,7'-OXYBIS[2,2-DIMETHYL-"
L4
L5
     (
```

12) SEA FILE=REGISTRY L4 OR L5 OR L6

14 SEA FILE=HCAPLUS L7

1 S L8 NOT L3

Inventor Seeser

### Reyes 10/018,617

#### => d l10 ibib abs hitstr 1

L10 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER:

DOCUMENT NUMBER:

2001:564976 HCAPLUS

135:122200

TITLE:

Preparation and characterization of alcohol and water

solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia, vascular disease and

diabetes

INVENTOR(S):

Ando, Howard Yoshihisa; Butler, Donald

Eugene; Dozeman, Gary Jay

PATENT ASSIGNEE(S):

Warner-Lambert Company, USA

SOURCE:

PCT Int. Appl., 81 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

Pront PATENT NO. KIND DATE APPLICATION NO. DATE -----\_\_\_\_ ----------WO 2001055078 A1 20010802 WO 2001-IB26 20010111 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG PRIORITY APPLN. INFO.: US 2000-177823P P 20000125

OTHER SOURCE(S):

MARPAT 135:122200

Alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2dimethylhexanoic acid monocalcium salt are prepd. which are cryst. and have the formula -02CC(CH3)2(CH2)4O(CH2)4CO2-.Ca2+.xR1OH(I; R1 = H, lower)alkyl, x = 0-10) [e.g., 6-(5-carboxy-5-methylhexyloxy)-2,2dimethylhexanoic acid monocalcium salt 1-Pr alc. solvate] and are useful for treating dyslipidemia, diabetes, and vascular disease; I-contg. formulations are presented.

ΙT 209789-08-2P

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(CI 1027; prepn. and characterization of alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia and vascular disease and diabetes)

RN 209789-08-2 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI)

Ca

# IT 351011-22-8P 351011-23-9P 351011-24-0P 351011-25-1P 351011-26-2P 351011-27-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and characterization of alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia and vascular disease and diabetes)

RN 351011-22-8 HCAPLUS

• Ca

● H2O

RN 351011-23-9 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with ethanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 64-17-5 CMF C2 H6 O

 ${\rm H_3C}-{\rm CH_2}-{\rm OH}$ 

RN 351011-24-0 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with methanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 67-56-1 CMF C H4 O

 ${\rm H3C-OH}$ 

RN 351011-25-1 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 1-propanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 71-23-8 CMF C3 H8 O  $_{\rm H3C-CH_2-CH_2-OH}$ 

RN 351011-26-2 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 2-propanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 67-63-0 CMF C3 H8 O

RN 351011-27-3 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 1-butanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 71-36-3 CMF C4 H10 O

 $_{\rm H3C-CH_2-CH_2-CH_2-OH}$ 

## Reyes 10/018,617

RN 1305-78-8 HCAPLUS

CN Calcium oxide (CaO) (9CI) (CA INDEX NAME)

Ca = 0

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

# => d 127 ibib abs hitstr 1-14

L27 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2002:446076 HCAPLUS

TITLE:

Process and polymer-based system for controlled-release drug delivery

INVENTOR(S):

Fessehaie, Mebrahtu; Ghebre-Sellassie, Isaac; Mollan,

Matthew Joseph, Jr.; Mayassi, Monzer Michael; Woldegaber, Haimanot; Dyar, Stephen Craig

PATENT ASSIGNEE(S):

Warner-Lambert Company, USA

SOURCE:

Eur. Pat. Appl., 14 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

Blate

KIND DATE APPLICATION NO. PATENT NO. DATE \_\_\_\_\_\_ \_\_\_\_\_\_ EP 1213014

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:

US 2000-251996P P 20001207

A controlled-release dosage form for a pharmaceutically-active agent comprises a core, in which the agent is dispersed, surrounded by a diffusion-limiting sleeve. The agent is released at a zero-order or approx. linear rate because the release rate of the agent will be governed entirely by erosion from exposed core surfaces; the surface area of which does not change substantially during the release process. Such a product may be made by coextruding the core and sleeve material and slicing the extrudate. For example, a compn. for exemplary coating material contained Eudragit RS 95.0% and tri-Et citrate 5.0%, and a compn. for the exemplary core material contained polyvinylpyrrolidone 43.5%, PEG 400 10%, and an active pharmaceutical ingredient, e.g., troglitazone 43.5%. Other active pharmaceutical ingredients used in prepn. of coextruded dosage forms were CI-1017 (an agent useful for treating Alzheimer's disease), CI-1011, an agent useful for regulating lipids in mammals, or CI-1027, an agent useful for treating diabetes and for elevating HDL-cholesterol in mammals.

ΙT **209789-08-2**, CI-1027

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prepn. of polymer-based controlled-release drug delivery system by core/coat coextrusion)

RN209789-08-2 HCAPLUS

Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) CN INDEX NAME)

Ca

L27 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2002:71865 HCAPLUS

DOCUMENT NUMBER:

136:112665

TITLE:

Treatment of eating disorders using carboxyalkyl

ethers

INVENTOR(S):

Auerbach, Bruce Jeffrey; Butler, Donald Eugene

PATENT ASSIGNEE(S):

Warner-Lambert Company, USA

SOURCE:

PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005807	A1	20020124	WO 2001-US16334	20010518

AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2000-218399P P 20000714

PRIORITY APPLN. INFO.: OTHER SOURCE(S):

MARPAT 136:112665

Carboxyalkylethers, e.g. 6-(5-carboxy-5-methyl-hexyloxy)-2,2dimethylhexanoic acid, are useful for treating eating disorders, e.g. obesity.

IT 209789-08-2, CI 1027

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(carboxyalkyl ethers for treatment of eating disorders)

RN 209789-08-2 HCAPLUS

Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) CN (CA INDEX NAME)

Ca

REFERENCE COUNT:

7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2002 ACS L27 ANSWER 3 OF 14 ACCESSION NUMBER: 2001:903813 HCAPLUS

DOCUMENT NUMBER:

136:15239

TITLE:

Carboxyalkyl ether-ACAT inhibitor combinations

INVENTOR(S):

Auerbach, Bruce Jeffrey; Zobel, Donna Lee

PATENT ASSIGNEE(S):

Warner-Lambert Company, USA

SOURCE:

PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

DATE PATENT NO. KIND APPLICATION NO. DATE \_\_\_\_\_ \_\_\_\_\_ WO 2001093845 A2 20011213 WO 2001-US14804 20010508 W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2000-210056P P 20000607

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 136:15239

A pharmaceutical compn. comprising (i) a carboxyalkyl ether which lowers triglycerides and LDL and elevates HDL, and (ii) an ACAT inhibitor which improves dyslipidemias in mammals, useful for treating dyslipidemia and ischemic syndromes, and for preventing or delaying the onset of heart attacks is described. A ACAT inhibitor is [(2,4,6triisopropylphenyl)acetyl]sulfamic acid 6-diisopropylphenyl ester (CI-1011) and a carboxyalkyl ether is 6,6'-oxybis(2,2-dimethylhexanoic acid) or its calcium salt. For example, the lipid modifying and antiatherosclerotic action of CI-1011, CI-1027, and the combination of both compds. was assessed in a rabbit cuff model of atherosclerosis.

IT 209789-08-2

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(CI 1027; carboxyalkyl ether-ACAT inhibitor combinations as antiatherosclerotic and hypocholesterolemic agents)

209789-08-2 HCAPLUS RN

Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA CN INDEX NAME)

Ca

HCAPLUS COPYRIGHT 2002 ACS L27 ANSWER 4 OF 14

ACCESSION NUMBER:

2001:798043 HCAPLUS

DOCUMENT NUMBER:

135:339248

TITLE:

INVENTOR(S):

Antihypertensive agents comprising carboxyalkylethers Auerbach, Bruce Jeffrey; Hitchcock, Karen Diane; Ryan,

Michael John

PATENT ASSIGNEE(S):

Warner-Lambert Company, USA

SOURCE:

PCT Int. Appl., 38 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2001080847 A2 20011101 WO 2001-US9088 20010322

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO:

US 2000-199855P P 20000426

US 2000-242280P P 20001020

OTHER SOURCE(S): MARPAT 135:339248

The invention is a pharmaceutical compn. comprising a carboxyalkylether of the formula Y1(R1)(R2)C (CH2)nO(CH2)mC(R3)(R4)Y2 wherein R1, R2, R3, and R4 include alkyl, alkenyl, and alkynyl, m and n are integers from 2 to 9, Y1 and Y2 include COOH, CHO, tetrazole, COOR5 where R5 is alkyl, alkenyl, or alkynyl, or a pharmaceutically acceptable salt thereof, and an antihypertensive agent, said compn. being useful for treating vascular diseases. The invention includes a method of treating hypertension comprising administering a carboxyalkylether. Antihypertensive effect of CI-1027 in combination with quinapril was shown in rats.

IT 209789-08-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(CI 1027; antihypertensive agents comprising carboxyalkylethers)

RN 209789-08-2 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)

Ca



L27 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:564976 HCAPLUS

DOCUMENT NUMBER:

135:122200

TITLE:

Preparation and characterization of alcohol and water

solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia, vascular disease and

diabetes

INVENTOR(S):

Ando, Howard Yoshihisa; Butler, Donald Eugene;

Dozeman, Gary Jay

PATENT ASSIGNEE(S):

Warner-Lambert Company, USA

SOURCE:

PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO. -----20010802 WO 2001055078 A1 WO 2001-IB26 20010111 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG PRIORITY APPLN. INFO.: US 2000-177823P P 20000125 OTHER SOURCE(S): MARPAT 135:122200 Alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2dimethylhexanoic acid monocalcium salt are prepd. which are cryst. and have the formula -02CC(CH3)2(CH2)4O(CH2)4CO2-.Ca2+.xR1OH(I; R1 = H, lower)alkyl, x = 0-10) [e.g., 6-(5-carboxy-5-methylhexyloxy)-2,2dimethylhexanoic acid monocalcium salt 1-Pr alc. solvate] and are useful for treating dyslipidemia, diabetes, and vascular disease; I-contg. formulations are presented.

209789-08-2P TT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(CI 1027; prepn. and characterization of alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia and vascular disease and diabetes)

RN 209789-08-2 HCAPLUS

Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) CN INDEX NAME)

D Ca

#### 351011-22-8P 351011-23-9P 351011-24-0P-IT 351011-25-1P 351011-26-2P 351011-27-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and characterization of alc. and water solvates of

6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia and vascular disease and diabetes)

RN 351011-22-8 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1), monohydrate (9CI) (CA INDEX NAME)

Ca

H20

RN 351011-23-9 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with ethanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 64-17-5 CMF C2 H6 O

H3C-CH2-OH

RN 351011-24-0 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with methanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 67-56-1 CMF C H4 O

 ${\rm H_3C-OH}$ 

RN 351011-25-1 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 1-propanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 71-23-8 CMF C3 H8 O

 $_{\rm H3C-CH_2-CH_2-OH}$ 

RN 351011-26-2 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 2-propanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 67-63-0 CMF C3 H8 O

RN 351011-27-3 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 1-butanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5 CMF C16 H30 O5

CM 2

CRN 71-36-3 CMF C4 H10 O

 ${\rm H_{3}C-CH_{2}-CH_{2}-CH_{2}-OH}$ 

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:725586 HCAPLUS

DOCUMENT NUMBER:

133:291122

TITLE:

Ether compounds, compositions, and uses thereof

INVENTOR(S): Dasseux, Jean-louis H.; Oniciu, Carmen D.

PATENT ASSIGNEE(S):

Esperion Therapeutics, Inc., USA

SOURCE:

PCT Int. Appl., 263 pp.

DOCUMENT TYPE:

CODEN: PIXXD2

LANGUAGE:

Patent English FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO. \_\_\_\_\_ 20001012 WO 2000-US8788 20000331 WO 2000059855 A1( AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, W: AE, AG, AL, AM, AI, AO, AZ, BB, BB, BG, BR, BI, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CL, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG 20000331 EP 1204626 20020515 EP 2000-921608 A1 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL US 6410802 B1 20020625 US 2000-540740 20000331 PRIORITY APPLN. INFO.: US 1999-127321P P 19990401 WO 2000-US8788 W 20000331

OTHER SOURCE(S): MARPAT 133:291122

AB The present invention relates to novel ether compds., compns. comprising ether compds., and methods useful for treating and preventing cardiovascular diseases, dyslipidemias, dysproteinemias, and glucose metab. disorders comprising administering a compn. comprising an ether compd. The compds., compns., and methods of the invention are also useful for treating and preventing Alzheimer's Disease, Syndrome X, peroxisome proliferator activated receptor-related disorders, septicemia, thrombotic disorders, obesity, pancreatitis, hypertension, renal disease, cancer, inflammation, and impotence. In certain embodiments, the compds., compns., and methods of the invention are useful in combination therapy with other therapeutics, such as hypocholesterolemic and hypoglycemic agents.

## IT 183293-88-1

RL: RCT (Reactant); RACT (Reactant or reagent)
 (prepn. of novel ether compds. and therapeutic and preventive uses
 thereof)

RN 183293-88-1 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, diethyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2000:227499 HCAPLUS

DOCUMENT NUMBER:

132:260690

TITLE:

Method using cholesterol-lowering agents for

preventing or delaying catheter-based

revascularization

INVENTOR(S):

Black, Donald Michael

PATENT ASSIGNEE(S):

Warner-Lambert Company, USA

SOURCE:

PCT Int. Appl., 32 pp.

DOCUMENT TYPE:

CODEN: PIXXD2

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	PATENT NO.			KII	D	DATE			APPLICATION NO. DATE								
WO	2000	01839	95	A.	1	2000	0406		W	0 19	99-U	51538	- <b>-</b> 85	1999	0708		
	W:	ΑE,	AL,	ΑU,	BA,	BB,	BG,	BR,	CA,	CN,	CU,	CZ,	EE,	GD,	GE,	HR,	HU,
		ID,	IL,	IN,	IS,	JP,	ΚP,	KR,	LC,	LK,	LR,	LT,	LV,	MG,	MK,	MN,	MX,
		NO,	NZ,	PL,	RO,	SG,	SI,	SK,	SL,	TR,	TT,	UA,	US,	UZ,	VN,	YU,	ZA,
		AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM							
,	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,
		ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,
		CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG					
AU	9949	750		A.	1	2000	0417		P	U 19	99-49	9750		1999	0708		
EP	1117	392		A.	1	2001	0725		E	P 19	99-93	3376	3	1999	0708		
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,
		IE,	SI,	LT,	LV,	FI,	RO										
BR	9914	098		A		2001	0731		Е	R 19	99-1	4098		1999	0708		
NO	2001	0016	15	Α		2001	0424		N	0 20	01-1	615		2001	0329		
PRIORIT	Y APP	LN.	INFO	. :				1	US 1	998-	1024	57 P	P	1998	0930		
								1	WO 1	999-	US15	385	W	1999	0708		

Aggressively lowering cholesterol in patients suffering from coronary AΒ artery disease prevents or delays the need for catheter-based revascularization. A cholesterol-lowering agent, e.g. an HMG-CoA reductase inhibitor such as atorvastatin, is used in an amt. effective to cause an aggressive lowering of LDL cholesterol.

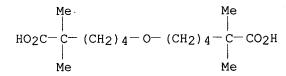
183293-82-5 ΙT

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cholesterol-lowering agents for preventing or delaying catheter-based revascularization)

183293-82-5 HCAPLUS RN

Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2002 ACS L27 ANSWER 8 OF 14 1999:495161 HCAPLUS ACCESSION NUMBER:

7

DOCUMENT NUMBER:

131:125474

TITLE:

Method for treating Alzheimer's disease with agents

lowering plasma triglycerides and optional

hypocholesterolemic agents

INVENTOR(S):

Bisgaier, Charles Larry; Emmerling, Mark Richard

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE:

PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	TENT	NO.		KI	ND	DATE			A	PPLI	CATI	ои ис	ο.	DATE			
WO WO	9938	498		 A	1	1999	0805		W W	0 19	98-U	S254:	95	1998	1202		
	W:	AL,	AU,	BA,	BB,	BG,	BR,	CA,	CN,	CU,	CZ,	EE,	GE,	HR,	ΗU,	ID,	IL,
														MX,			
														AM,			
		•	MD,	•	•			,	,	,	,		,	•	•		,
	RW:	•	,	•	•		SD.	SZ.	UG.	7.W.	AT.	BE.	CH.	CY,	DE.	DK.	ES.
	2													ВJ,			
		•	•		-					TD,		~_,	,	,	,	,	,
CA	2311	•	•	•		•	•			•		3113	56	1998	1202		
=	9916									U 19				1998			
	9814													1998			
	1051													1998			
E														NL,		MC	חים
	1.	•	•	•		FI,	•	ΙΙ,	GD,	GI,	ΤΤ,	DI,	шо,	ND,	UL,	110,	11,
TE	2002								-	P 20	00-5	2022	1	1998	1202		
										S 20				2001			
	2002								-				_				
PRIORIT	Y APP	LN.	TNFO	. :						998-			_	1998			
														1998			
OWITED C						יים ערכו	101			000-	5549	94	A3	2000	0523		

**\**05

OTHER SOURCE(S):

MARPAT 131:125474

AB A method for treating or preventing the onset of Alzheimer's Disease comprises administering to a mammal in need thereof an Alzheimer's Disease-preventing or -treating amt. of a plasma triglyceride level-lowering agent. Optionally, the plasma triglyceride level-lowering agent can be co-administered with a cholesterol level-lowering agent. The relationship between Alzheimer's disease and known risk factors for cardiovascular disease was also studied.

IT **209789-08-2**, CI 1027

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Alzheimer's disease treatment with plasma triglyceride-lowering agents and optional hypocholesterolemic agents)

RN 209789-08-2 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)

• Ca

REFERENCE COUNT:

THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1999:404834 HCAPLUS

131:49492 DOCUMENT NUMBER:

Statin-carboxyalkylether combinations for treating TITLE:

vascular diseases

Bisgaier, Charles Larry; Newton, Roger Schofield INVENTOR(S):

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.				KIND DATE				APPLICATION NO.						DATE			
WC	9930	704		A	1	1999	0624		N	0 19	98-U	S246	79	1998	1120		
	W:	AL,	ΑU,	BA,	BB,	BG,	BR,	CA,	CN,	CU,	CZ,	EE,	GE,	HR,	HU,	ID,	IL,
		IS,	JP,	KΡ,	KR,	LC,	LK,	LR,	LT,	LV,	MG,	MK,	MN,	MX,	NO,	ΝZ,	PL,
		RO,	SG,	SI,	SK,	SL,	TR,	TT,	UΑ,	US,	UZ,	VN,	YU,	ΑM,	ΑZ,	BY,	KG,
		KZ,	MD,	RU,	ТJ,	TM											
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SZ,	ÜG,	ZW,	AT,	BE,	CH,	CY,	DE,	DK,	ES,
		FI,	FR,	GB,	GR,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,
						ML,											
CF	2304	612		A	A	1999	0624		C	A 19	98-2	3046	12	1998	1120		
	9915																
BF	9813	542		Α		2000	1010		E	R 19	98-1	3542		1998	1120		
E	1045	691		A	1	2000	1025		E	P 19	98-9	6027	8	19983	1120		
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO										
JE	2002	5083	20	T	2	2002	0319		J	P 20	00-5	3868	7	1998	1120		
$z_{F}$	9811	348		Α		1999	0614		Z	A 19	98-1	1348		1998	1210		
NC	2000	0029	66	Α		2000	0609		N	0 20	00-2	966		20000	0609		
PRIORITY APPLN. INFO.:									US 1	997-	6937	5 P	Ρ	1997	1212		
								1	WO 1	998-	US24	679	W	1998	1120		

The invention is a pharmaceutical compn. comprising a carboxyalkylether AB which lowers triglycerides and elevated HDL, and a statin which inhibits HMG-CoA reductase, thereby reducing LDL, said compn. being useful for treating vascular diseases. Rats were fed with high cholesterol chow diet and were given 10 mg/kg of 6-6'-oxybis-(2,2-dimethylhexanoic acid calcium salt) and 30 mg/kg of atorvastatin calcium for 14 days. The triglyceride level and HDL/VLDL+LDL was 63 and 2.59 as compared with 118 mg/dL, and 2.59, resp., for the controls.

#### ΙT 209789-08-2

RN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(statin-carboxyalkylether combinations for treating vascular diseases) 209789-08-2 HCAPLUS

Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA CN INDEX NAME)

Ca

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2002 ACS L27 ANSWER 10 OF 14 1999:124309 HCAPLUS ACCESSION NUMBER:

2

DOCUMENT NUMBER:

130:305969

TITLE:

Automated solid-phase extraction workstations combined

with quantitative bioanalytical LC/MS

AUTHOR(S):

Huang, N. Helen; Kagel, John R.; Rossi, David T.

CORPORATE SOURCE:

Bioanalytical Core Group, Department of

Pharmacokinetics and Dynamics, Metabolism, Division of Warner-Lambert, Parke-Davis Pharmaceutical Research,

Ann Arbor, MI, 48105, USA

SOURCE:

Journal of Pharmaceutical and Biomedical Analysis

(1999), 19(3-4), 613-620 CODEN: JPBADA; ISSN: 0731-7085

Elsevier Science B.V.

DOCUMENT TYPE:

Journal

PUBLISHER: LANGUAGE:

English

An automated solid-phase extn. workstation was used to develop, AB characterize and validate an LC/MS/MS method for quantifying a novel lipid-regulating drug in dog plasma, i.e. PD 072953. Method development was facilitated by workstation functions that allowed wash solvents of varying org. compn. to be mixed and tested automatically. Precision ests. for this approach were within 9.8% relative std. deviation (RSD) across the calibration range. Accuracy for replicate detns. of quality controls was between -7.2 and +6.2% relative error (RE) over 5-1000 ng mL-1. Recoveries were evaluated for a wide variety of wash solvents, elution solvents and sorbents. Optimized recoveries were generally >95%. A sample throughput benchmark for the method was .apprxeq. 8 min per sample. Because of parallel sample processing, 100 samples were extd. in less than 120 min. The approach has proven useful for use with LC/MS/MS, using a multiple reaction monitoring (MRM) approach.

ΙT 183293-82-5, PD 72953

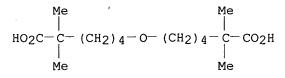
RL: ANT (Analyte); ANST (Analytical study)

(PD 072953 detn. in dog plasma using automated solid-phase extn.

workstations combined with quant. bioanal. LC/MS)

183293-82-5 HCAPLUS RN

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)





7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2002 ACS L27 ANSWER 11 OF 14 1998:374795 HCAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER: 129:62727

TITLE: A novel compound that elevates high density

> lipoprotein and activates the peroxisome proliferator activated receptor. [Erratum to document cited in

CA128:213102]

Bisgaier, Charles L.; Essenburg, Arnold D.; Barnett, AUTHOR(S):

Blake C.; Auerbach, Bruce J.; Haubenwallner, Sabine;

Leff, Todd; White, Andrew D.; Creger, Paul; Pape, Michael E.; Rea, Thomas J.; Newton, Roger S.

Division of Warner-Lambert Company, Departments of CORPORATE SOURCE:

VAscular and Cardiac Diseases, Ann Arbor, MI, 48105,

SOURCE: Journal of Lipid Research (1998), 39(6), 1317

CODEN: JLPRAW; ISSN: 0022-2275

PUBLISHER: Lipid Research, Inc.

Journal DOCUMENT TYPE: LANGUAGE: English

In the first column of Table 1, headed "Plasma Determinant," "ApoC-I"

should be "ApoC-II.". The cor. Table 1 is given. 171510-89-7, PD 72660 183293-82-5, PD 72953

IT

183293-83-6, PD 105726

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(PD 72953 and related compds. may reduce plasma triglycerides and apoB-contg. lipoprotein while raising HDL cholesterol via peroxisomal proliferation-activated receptors (Erratum))

171510-89-7 HCAPLUS RN

Pentanoic acid, 5,5'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME) CN

RN 183293-82-5 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)

183293-83-6 HCAPLUS RN

Heptanoic acid, 7,7'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME) CN

HCAPLUS COPYRIGHT 2002 ACS L27 ANSWER 12 OF 14

ACCESSION NUMBER:

1998:61642 HCAPLUS

DOCUMENT NUMBER:

128:213102

TITLE:

A novel compound that elevates high density

lipoprotein and activates the peroxisome proliferator

activated receptor

AUTHOR (S):

Bisgaier, Charles L.; Essenburg, Arnold D.; Barnett, Blake C.; Auerbach, Bruce J.; Haubenwallner, Sabine; Leff, Todd; White, Andrew D.; Creger, Paul; Pape,

Michael E.; Rea, Thomas J.; Newton, Roger S.

CORPORATE SOURCE:

Division of Warner-Lambert Company, Departments of Vascular and Cardiac Diseases, Ann Arbor, MI, 48105,

USA

SOURCE:

Journal of Lipid Research (1998), 39(1), 17-30

CODEN: JLPRAW; ISSN: 0022-2275

Lipid Research, Inc.

PUBLISHER: DOCUMENT TYPE:

Journal

English LANGUAGE:

In the current studies, the authors describe the effects of PD 72953 and related compds. on lipoprotein levels in chow-fed male rats. After 2 wk, 10 mg/kg of PD 72953 daily was as effective as 100 mg/kg gemfibrozil for elevating HDL-cholesterol. At 100 mg/kg, PD 72953 further elevated HDL-cholesterol to 232% of control levels, and was assocd. with increased HDL size and plasma apoE (169% of control), despite no change in hepatic apoE mRNA. ApoA-I rose transiently (at 1 wk), but by 2 wk only apoE remained elevated. PD 72953 dose-dependently reduced plasma apoB, VLDL-cholesterol, LDL-cholesterol, and triglyceride. Hepatic apoC-III mRNA redn. paralleled triglyceride lowering. After 1 wk, 30 and 100 mg/kg per day PD 72953 reduced plasma apoC-III levels by 30 and 34%, and triglycerides by 60 and 83%, resp. PD 72953 treatment had no effect on triglyceride prodn. rates; however, 125I-labeled VLDL apoB disappearance was enhanced. The authors compared PD 72953 to a structurally similarly diacid, PD 69405, that also reduced VLDL and LDL, but had no effect on HDL elevation. Compared to PD 72953, PD 69405 further accelerated 125I-labeled VLDL apoB disappearance, decreased triglyceride prodn., and elevated the ratio of post-heparin hepatic to lipoprotein lipase activity. Whole animal studies, transient transfection studies in HepG2 cells, and chimeric receptor studies in kidney 293 cells suggest that PD 72953 is a ligand for the peroxisomal proliferation activated receptor alpha (PPAR.alpha.), and PPAR.gamma.. Overall, PD 72953 may act through a peroxisomal proliferation-activated receptor and result in plasma triglycerides and apoB-contg. lipoprotein redn., while also raising HDL cholesterol. Reduced apoC-III may allow triglyceride-rich remnants to more efficiently bind and present substrate to peripheral tissue lipoprotein lipase, and therefore allow enhanced shedding of remnant phospholipid surface for HDL prodn.

171510-89-7, PD 72660 183293-82-5, PD 72953 183293-83-6, PD 105726 ΙT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(PD 72953 and related compds. may reduce plasma triglycerides and apoB-contg. lipoprotein while raising HDL cholesterol via peroxisomal proliferation-activated receptors)

171510-89-7 HCAPLUS RN

Pentanoic acid, 5,5'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME) CN

RN183293-82-5 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)

183293-83-6 HCAPLUS RN

Heptanoic acid, 7,7'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME) CN

HCAPLUS COPYRIGHT 2002 ACS L27 ANSWER 13 OF 14

1996:689457 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 125:328104

TITLE: Preparation of terminal carboxy or tetrazole

group-containing dialkyl ethers as anticholesteremics

and antidiabetics

Bisgaier, Charles Larry; Creger, Paul Leroy; Saltiel, INVENTOR(S):

Alan Robert; Tafuri, Sherrie Rae

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9630328	A1	19961003	WO 1996-US1639	19960205
W: AM,	AU, BG, BY	, CA, CN, CZ,	EE, FI, GE, HU, JP	, KG, KR, KZ, LT,
LV,	MD, MX, NO	, NZ, PL, RO,	RU, SG, SI, SK, TJ	, UA, UZ
RW: AT,	BE, CH, DE	, DK, ES, FR,	GB, GR, IE, IT, LU	, MC, NL, PT
US 5648387	A	19970715	US 1995-409780	19950324

```
AΑ
                             19961003
                                            CA 1996-2215233
                                                              19960205
    CA 2215233
    AU 9647768
                       Α1
                             19961016
                                            AU 1996-47768
                                                              19960205
                       B2
                             19980604
    AU 692359
                             19980128
                                            EP 1996-903794
                                                              19960205
    EP 820428
                       Α1
     EP 820428
                       В1
                             20000510
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV
     CN 1182415
                       Α
                             19980520
                                            CN 1996-193500
                                                              19960205
                                            JP 1996-529342
     JP 11502532
                       T2
                             19990302
                                                              19960205
                                            AT 1996-903794
    AT 192732
                             20000515
                       Ε
                                                              19960205
    ES 2148733
                                            ES 1996-903794
                       Т3
                             20001016
                                                              19960205
                       В1
                                            PL 1996-322407
                                                             19960205
     PL 181673
                             20010831
                                            CZ 1997-2922
    CZ 289556
                       В6
                             20020213
                                                              19960205
     ZA 9602275
                                            ZA 1996-2275
                       Α
                             19960930
                                                              19960320
     US 5750569
                                            US 1997-805533
                       Α
                             19980512
                                                              19970225
                                            US 1997-806582
     US 5756544
                       Α
                             19980526
                                                              19970225
                                            US 1997-806580
     US 5783600
                       Α
                             19980721
                                                              19970225
     FI 9703713
                       Α
                             19970924
                                            FI 1997-3713
                                                              19970917
                                            NO 1997-4397
     NO 9704397
                       Α
                             19971120
                                                              19970923
PRIORITY APPLN. INFO .:
                                         US 1995-409780
                                                           Α
                                                              19950324
                                         WO 1996-US1639
                                                           W 19960205
```

OTHER SOURCE(S): MARPAT 125:328104

The title compds. Y1(R1)(R2)C(CH2)nO(CH2)mC(R3)(R4)Y2 [I; R1-R4 = alkyl, alkenyl, alkynyl; Y1, Y2 = CO2H, CHO, tetrazole, (un)substituted carboxylate ester; m, n = 2-9], which lower Lp(a) and triglycerides and elevate HDL-cholesterol, useful for treating vascular diseases and noninsulin-dependent diabetes mellitus, are prepd. and I-contg. formulations presented. Thus, isobutyric acid was reacted with 4,4'-dichlorobutyl ether in the presence of (MeHC)2 and NaH, producing 6,6'-oxybis(2,2-dimethylhexanoic acid), m.p. 49-51.degree., which demonstrated anticholesteremic activity.

IT 171510-89-7P 183293-82-5P 183293-83-6P

183293-87-0P 183293-88-1P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of terminal carboxy or tetrazole group-contg. dialkyl ethers as anticholesteremics and antidiabetics)

RN 171510-89-7 HCAPLUS

CN Pentanoic acid, 5,5'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)

RN 183293-82-5 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)

183293-83-6 HCAPLUS RN

CN Heptanoic acid, 7,7'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)

RN 183293-87-0 HCAPLUS

CN Pentanoic acid, 5,5'-oxybis[2,2-dimethyl-, diethyl ester (9CI) (CA INDEX

RN 183293-88-1 HCAPLUS

Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, diethyl ester (9CI) (CA INDEX CN

HCAPLUS COPYRIGHT 2002 ACS L27 ANSWER 14 OF 14

1995:803901 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 124:29095

TITLE: Synthesis of 5,5,10,10-tetramethyl-1-oxacyclotridecane-

6,7,8,9-tetrone - on the mechanism of the Rubottom

reaction

Gleiter, Rolf; Staib, Michael; Ackermann, Uwe AUTHOR(S):

CORPORATE SOURCE: Organisch-Chemisches Inst. Univ. Heidelberg,

Heidelberg, D-69120, Germany

Liebigs Ann. (1995), (9), 1655-61 CODEN: LANAEM; ISSN: 0947-3440 SOURCE:

DOCUMENT TYPE: Journal

LANGUAGE: English

CASREACT 124:29095 OTHER SOURCE(S):

GI.

# \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The synthesis of 5,5,10,10-tetramethyl-1-oxacyclotridecane-6,7,8,9-tetrone (12) was achieved via a multistep procedure involving an oxidn. known as the Rubottom reaction. The key intermediates were the dialdehyde (I), the diacid (II), the cyclic diketone (III) and the bis(silyl enol ether) (IV). The oxidn. of IV with mCPBA yielded two diastereomeric hydroxy ketones , V (R = .alpha.-OH, .beta.-OH), the ratio of which depends strongly on the solvent used. This result combined with the isolation of the diepoxide (VI) gives an insight into the stereochem. of the Rubottom reaction. 171510-89-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of tetramethyl-1-oxacyclotridecanetetrone and mechanism of
 Rubottom reaction)

RN 171510-89-7 HCAPLUS

ΙT

CN Pentanoic acid, 5,5'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)